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Tuning indirect predictions based on SNP effects from ssGBLUP

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Why Indirect predictions?

- Interim evaluations
 - Between official runs
- Not all genotyped animals are in the evaluations
 - Animals with incomplete pedigree increase bias and lower R^2
- Commercial products
 - e.g. GeneMax for non-registered animals

Indirect predictions in ssGBLUP

$$\begin{bmatrix} \mathbf{X}'\mathbf{X} & \mathbf{X}'\mathbf{W} \\ \mathbf{W}'\mathbf{X} & \mathbf{W}'\mathbf{W} + \mathbf{H}^{-1}\lambda \end{bmatrix} \begin{bmatrix} \hat{\mathbf{b}} \\ \hat{\mathbf{u}} \end{bmatrix} = \begin{bmatrix} \mathbf{X}'\mathbf{y} \\ \mathbf{W}'\mathbf{y} \end{bmatrix}$$

$$\mathbf{DGV} = \mathbf{Z}\hat{\mathbf{a}}$$

$$\hat{\mathbf{a}} = \lambda \mathbf{D} \mathbf{Z}' \mathbf{G}^{-1} \hat{\mathbf{u}}$$

SNP effects GEBVs

$$\mathbf{GEBV}_{\text{young}} = w_1 \mathbf{PA} + w_2 \mathbf{DGV} - w_3 \mathbf{PP}$$

$$\mathbf{GEBV}_{\text{young}} \approx \mathbf{DGV} = \mathbf{Z}\hat{\mathbf{a}}$$

$$\mathbf{H}^{-1} = \mathbf{A}^{-1} + \begin{bmatrix} 0 & 0 \\ 0 & \mathbf{G}^{-1} - \mathbf{A}_{22}^{-1} \end{bmatrix}$$

$$\mathbf{G}_{\text{APY}}^{-1}$$

Lourenco et al., 2015

Problems with Indirect predictions

**Genetic evaluation using single-step genomic best linear unbiased predictor
in American Angus¹**

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$$\text{COR}(\widehat{\text{GEBV}}, \mathbf{Z}\hat{a}) > 0.99$$

$$\text{Avg}(\widehat{\text{GEBV}}) \approx 100 \quad \neq \quad \text{Avg}(\mathbf{Z}\hat{a}) \approx 0$$

Objectives

- 1) Fine-tune indirect predictions to be compatible with GEBV
- 2) Investigate whether SNP effects are accurate when APY is used
 - Possibly use subset of core animals

Dataset

- American Angus Association
 - 8.2M animals in pedigree
 - 6.2M birth weight (BW)
 - 6.8M weaning weight (WW)
 - 3.4M post-weaning gain (PWG)
 - 81k genotyped
 - born 1977-2012: 66k
 - born 2013-2014: 15k
- Complete
 - Phenotypes up to 2012
 - Genotypes up to 2014 (81k)
- Reduced
 - Phenotypes up to 2012
 - Genotypes up to 2012 (66k)
- 3-trait with mat and mpe
- Results for PWG

Accuracy of SNP effects from \mathbf{G}_{APY}^{-1} or \mathbf{G}_{CC}^{-1}

$$\hat{\boldsymbol{a}}_{\mathbf{G}} = \lambda \mathbf{D} \mathbf{Z}' \mathbf{G}^{-1} \hat{\boldsymbol{u}}$$

$$\hat{\boldsymbol{a}}_{\mathbf{G}_{APY}^{-1}\mathbf{H}} = \lambda \mathbf{D} \mathbf{Z}' \mathbf{G}_{APY_high_reliability}^{-1} \hat{\boldsymbol{u}}_{APY}$$

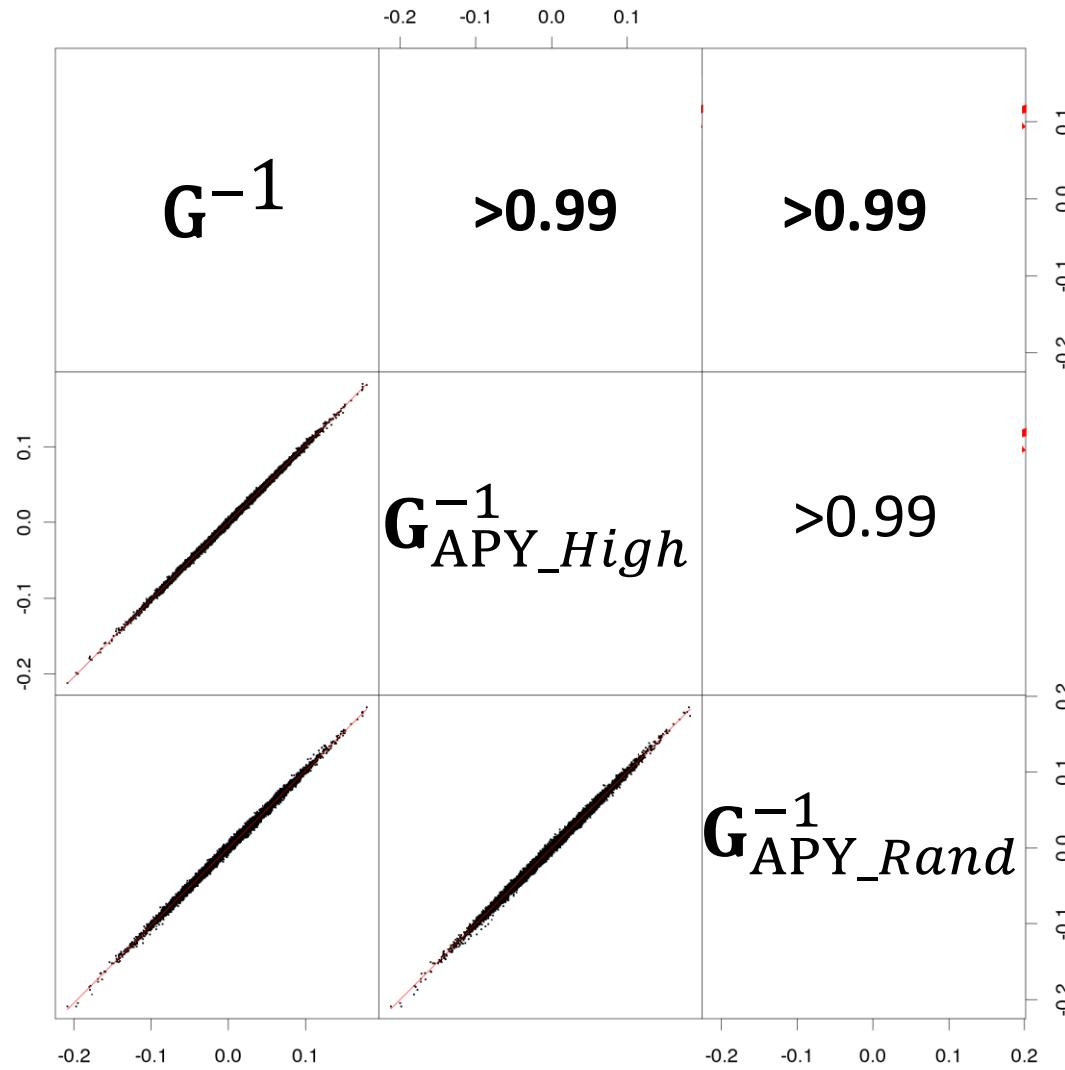
$$\hat{\boldsymbol{a}}_{\mathbf{G}_{APY}^{-1}\mathbf{R}} = \lambda \mathbf{D} \mathbf{Z}' \mathbf{G}_{APY_random}^{-1} \hat{\boldsymbol{u}}_{APY}$$

$$\hat{\boldsymbol{a}}_{\mathbf{G}_{CC}^{-1}\mathbf{H}} = \lambda \mathbf{D} \mathbf{Z}' \mathbf{G}_{CC_high_reliability}^{-1} \hat{\boldsymbol{u}}_{APY}$$

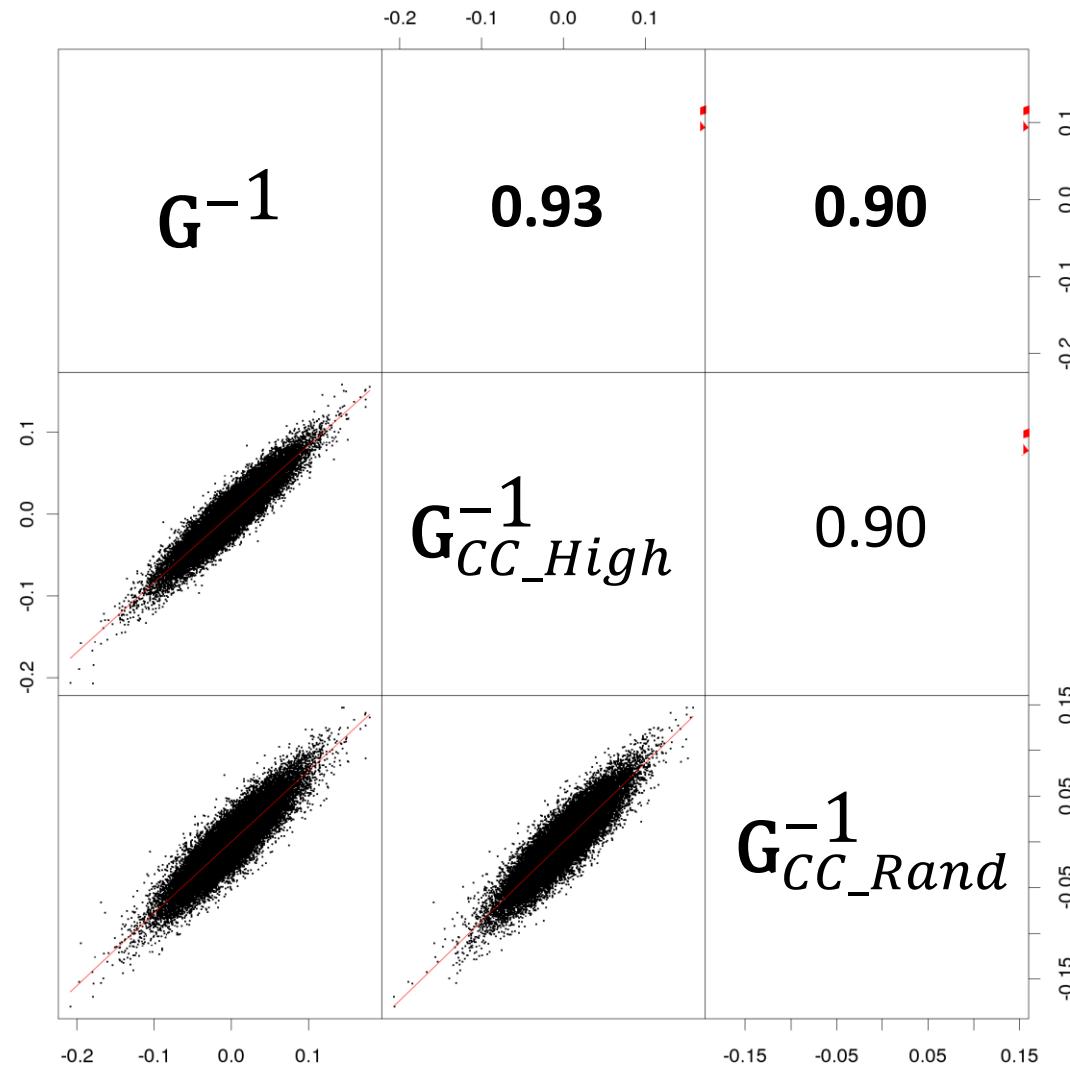
$$\hat{\boldsymbol{a}}_{\mathbf{G}_{CC}^{-1}\mathbf{R}} = \lambda \mathbf{D} \mathbf{Z}' \mathbf{G}_{CC_random}^{-1} \hat{\boldsymbol{u}}_{APY}$$

- Correlation between SNP effects
- Correlation between $\mathbf{Z}\hat{\boldsymbol{a}}$

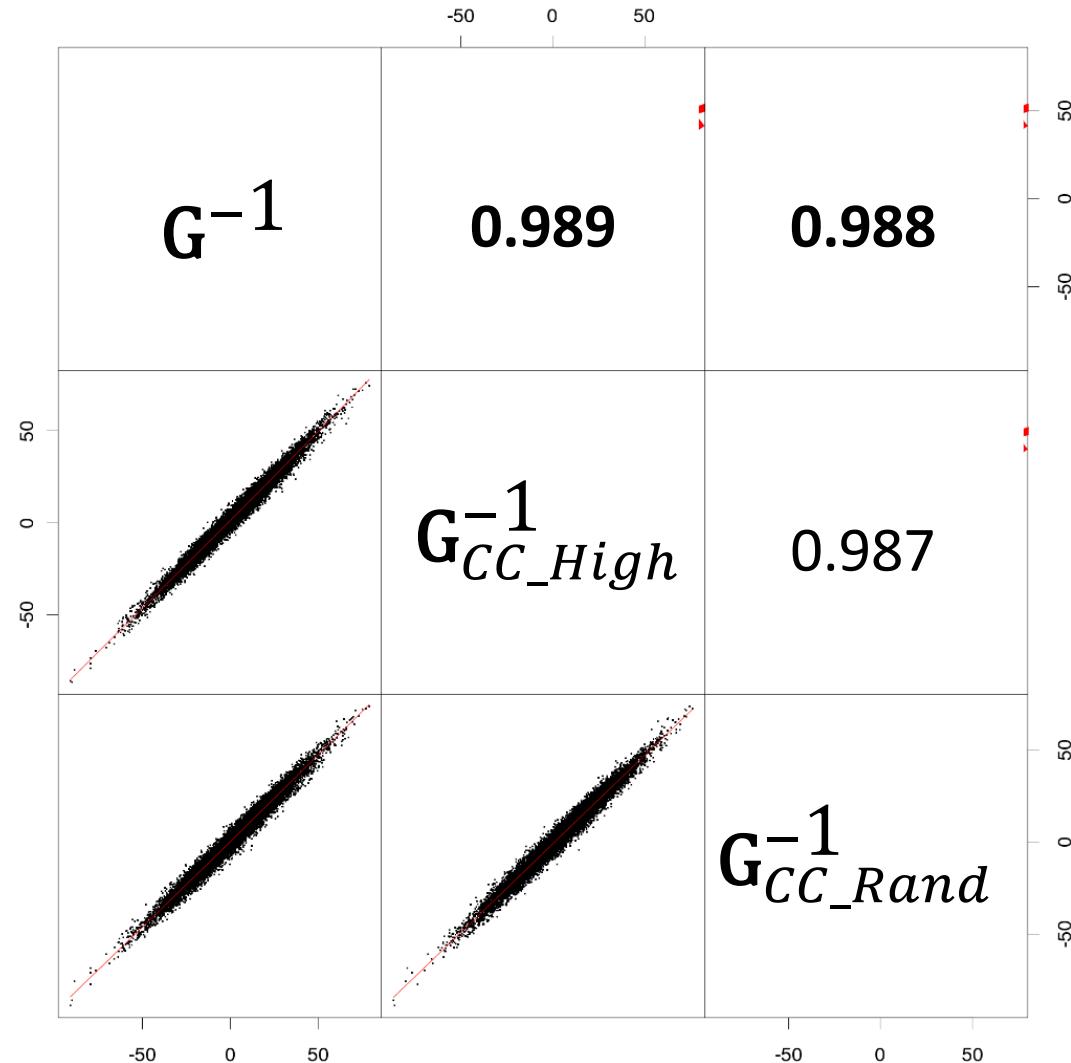
Statistics for SNP effects



Statistics for SNP effects



Statistics for $\hat{Z}\hat{a}$



Fine-tuning indirect predictions from ssGBLUP

Understanding genetic and genomic bases

- Base of BLUP: *founders of the pedigree*
- Base of GBLUP: *genotyped animals*
- Base of SSGBLUP: Vitezica et al. (2011) modeled as a mean in genotyped animals
 - $p(\mathbf{u}_g) = N(\mathbf{1}\mu, \mathbf{G})$
 - $\mu = (\text{Pedigree base}) - (\text{Genomic base})$

Fine-tuning indirect predictions from ssGBLUP

1) Formula in Legarra (2017)

$$\hat{\boldsymbol{u}}_{ip} = \hat{\mu} + 0.95 \mathbf{Z} \hat{\boldsymbol{a}} + 0.05 \hat{\boldsymbol{u}}_{parents}$$

SNP and
pedigree
fractions

2) Double fitting

a) fit a regression using genotyped animals in the evaluation

$$DGV_{eval} = b_0 + b_1 \mathbf{Z} \hat{\boldsymbol{a}}$$

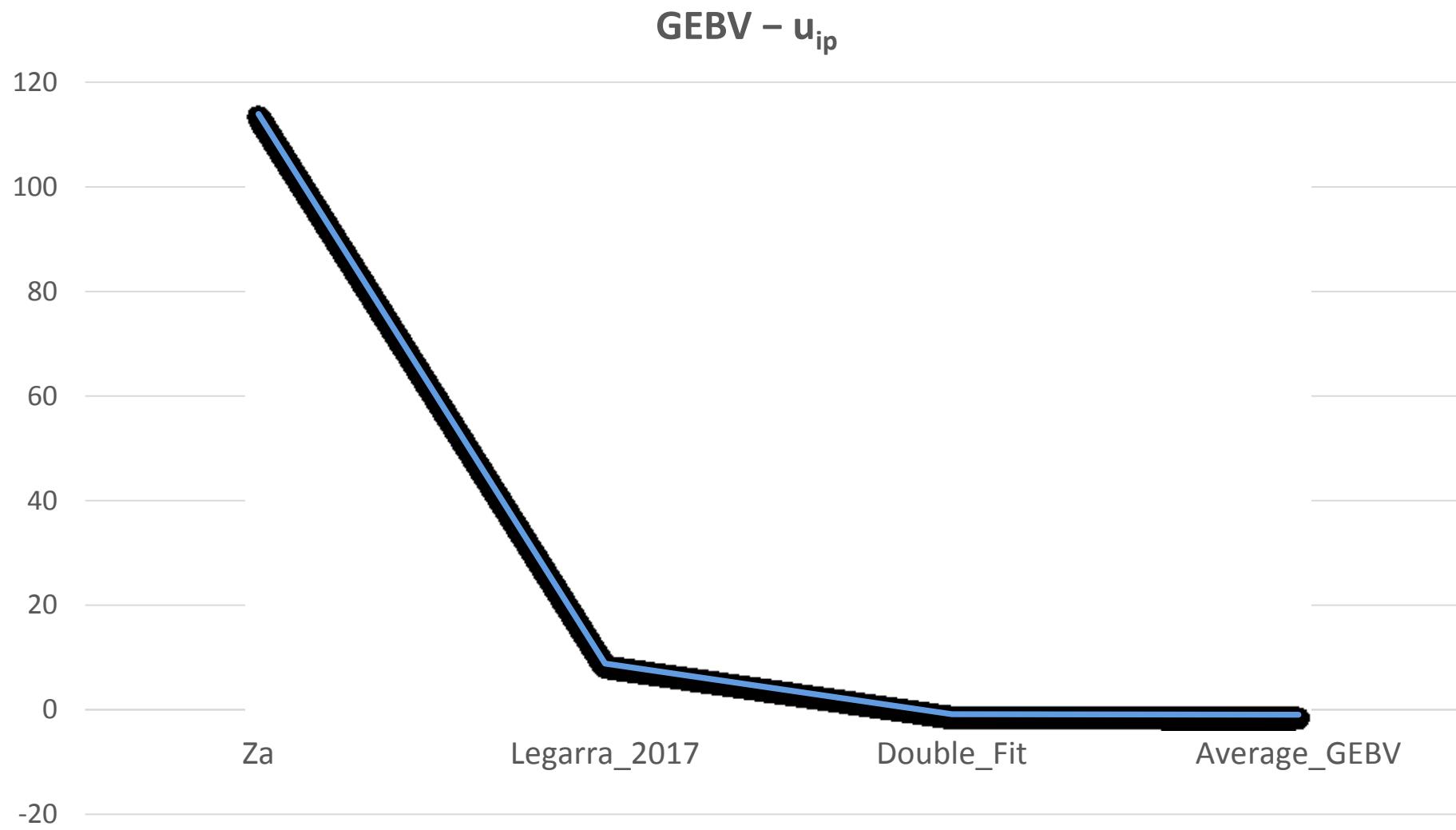
b) apply regression for indirectly predicted animals

$$\hat{\boldsymbol{u}}_{ip} = b_0 + b_1 \mathbf{Z} \hat{\boldsymbol{a}}$$

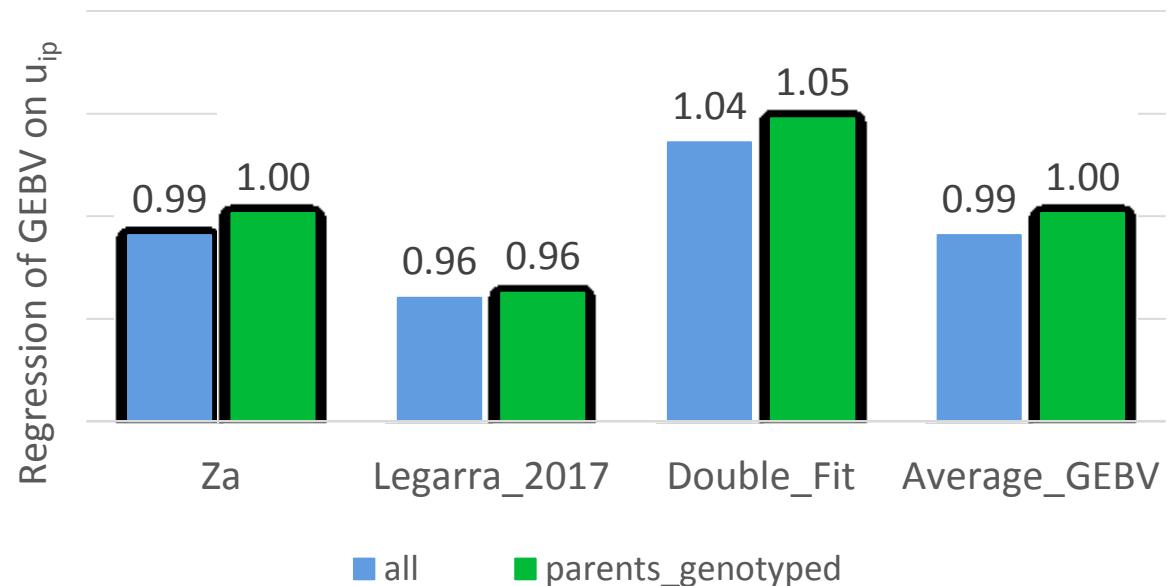
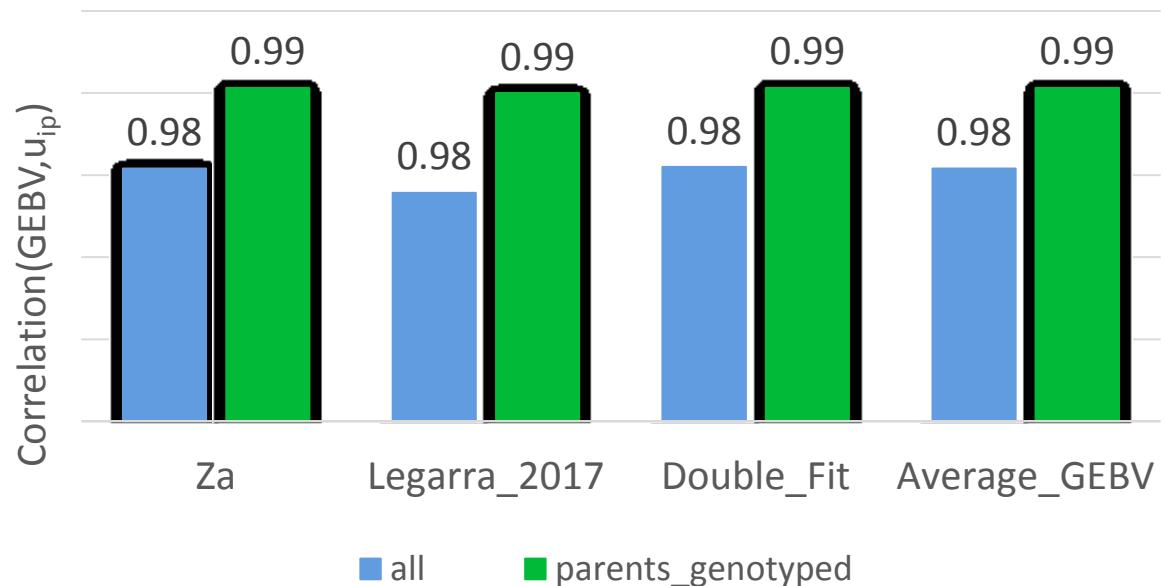
3) Add average GEBV

$$\hat{\boldsymbol{u}}_{ip} = \overline{GEBV}_{eval} + \mathbf{Z} \hat{\boldsymbol{a}}$$

Bias of indirect predictions



Correlation & Regression Coefficient



Fine-tuning indirect predictions in ssGBLUP

$$E(\hat{u}|\hat{a}) = \mu + \mathbf{z} \frac{\mathbf{1}}{2 \sum p(1-p)} \left(\mathbf{I} \frac{\mathbf{1}}{2 \sum p(1-p)} \right)^{-1} (\hat{a} - 0)$$

$$E(\hat{u}|\hat{a}) = \mu + \mathbf{z}\hat{a}$$

\approx

$$E(\hat{u}|\hat{a}) = \overline{GEBV} + \mathbf{z}\hat{a}$$

Final Remarks

- Indirect predictions are unbiased after corrections
 - Can be used as interim evaluation
- Indirect predictions based on core animals are slightly less accurate
 - Reduction in computing time (no G_{nc}^{-1} and G_{nn}^{-1})
- SNP effects from ssGBLUP may be useful for SNP MACE

Acknowledgements

